CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

http://proteomics.cancer.gov

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MS VENDOR ORIENTATION MEETING (RFA-CA-07-012)

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Today's Agenda

- Government / Industry Partnerships
- Challenges of Clinical Proteomics
- Clinical Proteomic Technologies Initiative (CPTI) Core Programs
- Clinical Proteomic Technology Assessment for Cancer Teams (CPTACs): Role, Key Features, and Goals
- Role and Benefit to Technology Providers

Government / Industry Partnerships

- **NCI's Office of Technology and Industrial Relations (OTIR) focuses on technology-based initiatives to accelerate the creation and use of tools that will bring a new generation of molecular-based diagnostics and therapeutics to the clinic**

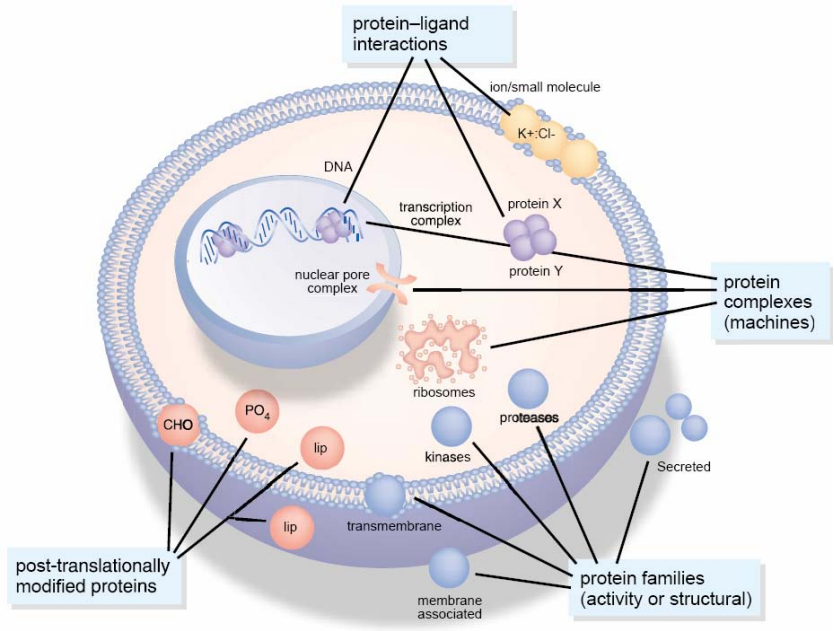
- **OTIR encourages new technology development and promotes collaborations between NCI and the private sector**

- **Purpose of teleconference:**
  - Present NCI's Clinical Proteomic Technologies Initiative
  - Reinforce the need for collaboration of MS technology developers with NCI scientists and program investigators to advance proteomics from a research tool to clinical application

Clinical Proteomics Today

- **No** single technology platform can satisfy all of the desired proteomic measurements

- **No** shared performance criteria
  - Poor confidence in protein measurement results
  - Difficulty in assessing agreement of different experiments
  - Conflicting reports in the literature
  - Lost opportunities



Scott D. Patterson & Ruedi H. Aebersold, Proteomics: the first decade and beyond, *Nature Genetics* 33, 311-323 (2003)

Community Input and Consensus

- **On the basis of discussions with a wide range of clinicians, cancer researchers, and technologists, the NCI recognized that there are immense opportunities for using proteomic technologies to solve mission-critical problems in cancer research.**

- **Premises:**
  - Proteins/peptides exist in readily accessible body fluids that can serve as useful indicators of a disease state
  - Profiles of such proteins/peptides can be used for diagnostic/clinical purposes
  - Panels of such markers will be required to achieve high specificity and sensitivity
  - Current technology is capable of discovering these panels
  - Current application of this technology to discovery can be improved

Sources of Variability in Existing Proteomic Technologies

- **Specimen handling and processing**
- **Platform evaluation**
  - Technical (resolution, accuracy, dynamic range, sensitivity, reproducibility)
  - Cross verification among platforms
- **Data acquisition/Bioinformatics**
- **Data analysis**
- **Publication uniformity**

Goal: Assurance that protein measurement results are due to changes in the sample and not changes or variability due to:

- Instrument
- Assay performance
- Reagents
- Operator
- Site

Challenges to the Clinical Measurement of Proteins

- **Pervasive problems with research design, data analysis, reproducibility, and comparability of research results**
- **Lack of common reagents and highly qualified public data sets**
- **Ineffective and inefficient transfer of platform technologies to clinical application (technology gap)**
- **Inability to manage and interpret large quantities of pre-processed data**

NCI is uniquely positioned to help the scientific community and technology providers address these challenges:

- Integration with NIH institutes
- Clinical trials
- Collaborations with industry and other organizations
- Translation into practice

Overcoming Challenges in Proteomics: NCI Clinical Proteomic Technologies Initiative for Cancer (CPTI)

- **Scope:** 5-year, $104M
- **Objective:** Integrated approach to assess, enhance and develop proteomic technology measurement capabilities
- **Key Components:**
  - Build a multidisciplinary team framework
  - Refine and standardize technologies, and statistical/analytical methods
  - Develop and evaluate new technical approaches
- **Scientific Goals:**
  - Build a foundation of technologies; data; reagents and reference materials; analysis systems; and infrastructure
  - Systematically advance understanding of protein biology in cancer
  - Accelerate discovery research and clinical proteomics

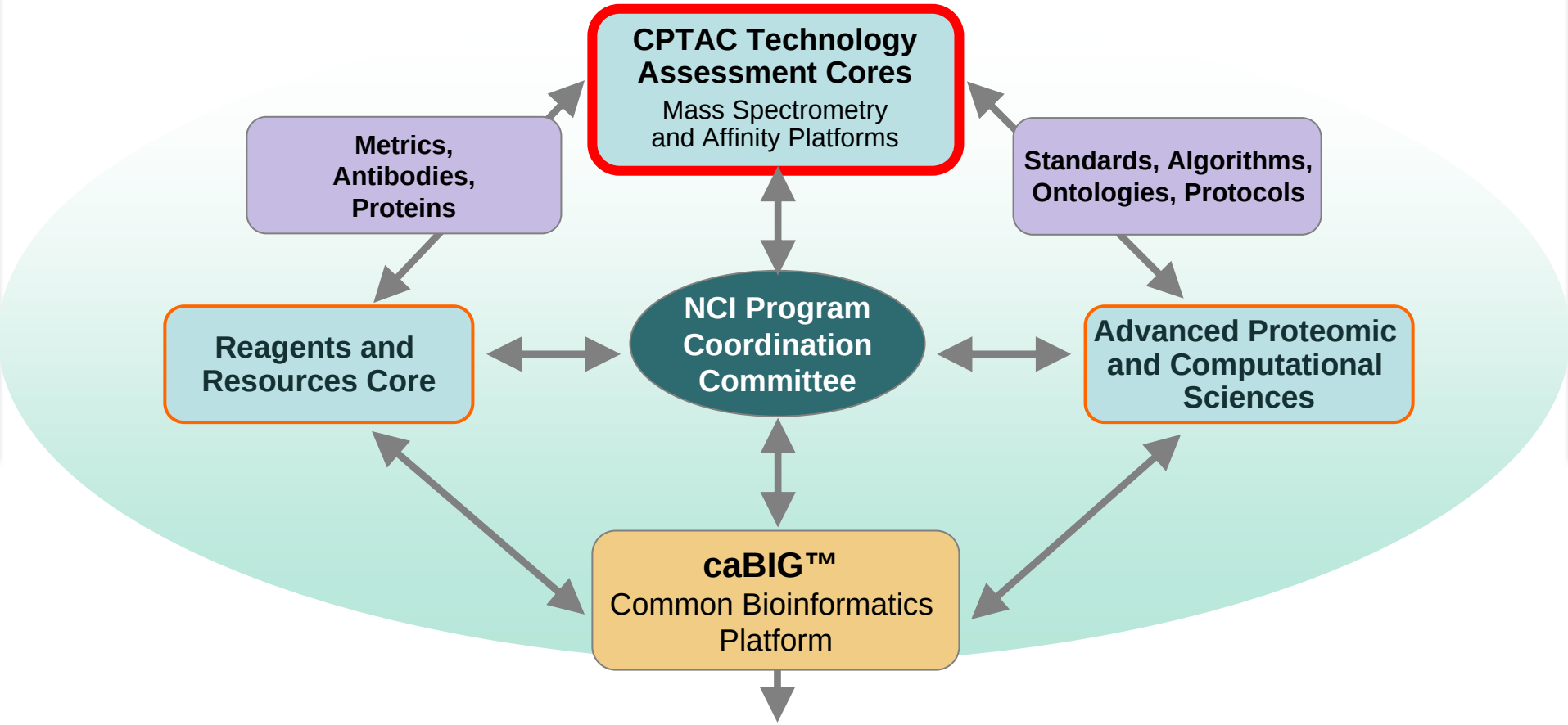
Components of CPTI Program

1. **Clinical Proteomic Technology Assessment for Cancer (CPTAC) (RFA-CA-07-012)**
   - Evaluate existing proteomic analysis platforms to reliably identify, quantify, and compare peptides/proteins in complex biological mixtures
   - Mass spectrometry and Affinity-based technologies
   - Multidisciplinary Team approach

2. **Advanced Proteomic Platforms and Computational Sciences (RFA-CA-07-005)**
   - Support highly innovative research in the “quantitative” analysis of peptides/proteins of interest in clinical cancer studies

3. **Clinical Proteomic Reagents Resource**
   - Proteins, peptides, antibodies, proficiency testing materials, and informatics

Clinical Proteomic Technologies Initiative Strategy



- Integrated Searchable Proteomic Database
- Highly Qualified Biospecimens
- Standardized Reagents
- Optimized Technology Platforms
- Proteomic Standards
- New Technologies

Objectives of the CPTAC Program

- **Objective 1:** Evaluate performance of proteomic technology platforms and standardize approaches to developing applications using these platforms;
- **Objective 2:** Evaluate proteomic platforms for their ability to analyze cancer-relevant proteomic changes in human clinical specimens;
- **Objective 3:** Establish systematic ways to standardize proteomic protocols and data analysis among multiple laboratories;
- **Objective 4:** Develop and implement uniform algorithms for sharing bioinformatics and proteomic data and analytical/data mining tools across the scientific community;
- **Objective 5:** Develop well-defined and comprehensively characterized sets of standard/reference materials and reagents to serve as resources for the research community.

Mass Spec Platforms - Configurations

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Mass Resolution - ability to discriminate between two m/z values that are close to one another

Mass Accuracy - true m/z value of the particle of interest

Mass Range - the high and low m/z values that can be detected

Instrument Sensitivity - minimal amount of analyte that can be detected

Protein/Peptide ID Mass Spec Technologies

Peptide/Protein ID

1 Protein Separation

- 1-D LC
- 2-D LC
- Microfluidics/LC
- Affinity columns (e.g. Ab)
- Affinity capture (non-Ab)

2 Ion Source

- ESI
- MALDI

3 Mass Analyzer

- Ion Trap
- Triple Quadrupole
- QTOF
- FTICR
- TOF
- TOF/TOF

Role and Benefit to Technology Providers in CPTAC

- **Are full collaborative partners with CPTI/NCI, CPTAC research teams**
- **Help formulate direction and planning for assessment of technologies**
- **Provide technical expertise and direction on optimal use of technology platforms (provider in-house teams critical to success)**
- **Take insights generated by CPTAC back into platform development process to maximize utility**
- **Have immediate access to CPTAC methodologies and data that can inform vendor-directed use of platforms by all users/customers**
- **Existing Collaborations:**
  - National Institute of Standards and Technology
  - Argonne National Laboratory
  - European Bioinformatics Institute

Communication to Stakeholders

- Archived viewing is available through the website http://proteomics.cancer.gov
- Email questions to cancer.proteomics@mail.nih.gov

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Website: http://proteomics.cancer.gov

Questions

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